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Formulation and evaluation of papaya leaves used for the treatment of dengue

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Abstract
To formulate and evaluate papaya leaves and euphorbia hitra by using different sweetening agents like sucrose, maltose, sucralose and saccharin etc. Medicinal plants such as *Carica papaya,* and *Euphorbia hitra,* is an ever green medicinally useful tree that tolerates various stress of the desert. Medicinal plants have been a variable source of natural activity phytochemical constituents that play an important role in the treatment of many human diseases. In the present study, leaves of *Carica papaya, euphorbia hitra* was by its Anti-bacterial activity the qualitative phyto-chemical analysis and bacterial potential. The extraction was done by using soxhlation process. The prepared poly herbal syrup were evaluated such as color, odour, taste pH, specific gravity, viscosity. The Anti-bacterial activity was evaluated by cup plate method against different pathogenic Gram negative and Gram-positive bacteria. The abstractive yield was maximum in methanol extraction with *papaya and euphorbia hitra,* leaves etc., The prepared were evaluated for the polyherbal syrup by In-vitro permeation studies using dialysis membrane, among all the 6 formulations F6 formulation was shown 84.8% cumulative drug release within 8 hours.

Keywords: carica papaya leaves, euphorbia hitra, poly herbal syrup, gram negative, gram positive bacteria, dialysis membrane

1. Introduction: Dosage Forms

There are different forms into which a drug may be placed (regulated/given or taken) for convenient and effective treatment of disease. Drugs can be prepared for administration by very conceivable route and the suitable preparation is formulated to insure maximum therapeutic response. These are the pharmaceutical drug products in the form of medicinal use such as syrups, suspensions lozenges, creams, pastes, aerosols, sprays, lotions, elixirs, gels, powders, troches or lozenge, ointments, creams, pastes, aerosol, lotions, sprays, inhalants, emulsions and suppositories. The preferred dosage forms in different routes of administration is listed [1].

Types of dosage forms [2]

There are different types dosage forms available for convenient and effective treatment.

1. Intraocular Solutions and Suspensions
2. Intranasal Solutions, Ointments Aersol, Sprays Inhalants
3. Intrarespiratory Aerosol
4. Rectal Solutions, Ointments Suppositories
5. Vaginal Tablets, Solutions, Ointments, Emulsions and Suppositories
6. Urethral Solutions and Suppositories

Advantages of oral route of administration [3]

1. It is most easy route for administration of drug for patients.
2. It is the safest route of administration.
3. It is most convenient for patients.
4. This route can be used for large variety of dosage . forms.
5. Nursing for administration is not required.
6. An allergic reaction of drug is delayed and hence safe.
7. It is economical to the patients.

Disadvantages of oral route of administration

1. The onset of action of drug is late and hence it is not fast. In emergency condition oral administration was not used.
2. when the gastrointestinal tract the dose of drug absorbed is more.
3. It is difficult route of administration of drug for non-cooperative patients like babies
4. and children.
5. It is difficult route of administration of drug for un cooperative patients.
6. The absorption of drug from gastrointestinal tract is not imperturbable by patients suffering from gastrointestinal disorder.
7. Oral route of administration may cause gastrointestinal disorders like acidity, loss of
8. appetite, etc.
9. The maintanance of the dose of drug is possible in oral route of administration.
10. Drug may be inactivated by the enzyme in gastrointestinal tract.

Liquid Dosage Forms [4]

Liquid dosage forms are a drug used as medication intended for teasaurus. Liquid dosage forms are classified into two types Monophasic liquid dosage forms. Biphasic liquid dosage forms.

Monophasic Liquid Dosage Forms

It contains only one phase. They are divided into two types.

a. liquids for internal use: drops, Elixirs, linctus, Syrups, and Draughts.
b. B. liquids for external use: Linements, and Lotions.

Biphasic Liquid Dosag Form

It contains two types

a. Suspensions
b. Emulsions

Syrups [5]

Syrups are concentrated, aqueous preparations of a sugar containg a thick sweet liquid by dissolving sugar in boiling water. e.g. Corn syrup, glucose syrup.

Components of syrup

Most of the syrups containing the addition to be purified by water and ayurvedic agents

1. Sugars are usually a preservative fruit contains sweetening agents.
2. Antimicrobial preservatives are flavanoids and colourants.

Sucrose and non-sucrose-based syrup

It may be commonly recruit in syrups. In circumstances it may be replaced by maltose, sucrose, as sorbitol.

Methyl cellulose absorbed into the blood stream and use results in an excellent syrup like vehicle.

Taste masking by syrup

The syrup imparts a characteristics "body" and together with the flavourants in the preparation of effective masking and also the taste is added in to the medicinal agents. When the syrup is swallowed, into a dissolved drug and it makes touch with the taste buds. and the solution may be carried through the throat which is contaminated due to the viscous syrup. it may also known as anti tussive syrup.

Preparation of Syrups

Depending upon the physical and chemical characteristics syrups was prepared by four general methods.

1. Solution may be due to assistance of heat.
2. Solution by concern without the use of heat.
3. Addition of maltose to be prepared by flavored liquid.
4. By filtration method the source of the medicating substance of the sucrose.

Solution with the aid of heat

When heat is applied in the preparation of sucrose syrup, some inversion of the sucrose is almost certain. The speed of inversion is greatly increased by the presence of acids, the hydrogen ion acting as a catalyst to reaction. Invert sugar is sweeter than sucrose is colour less. Due to the effect of heat on the fructose the syrup is overheated and becomes caramelize of the sucrose.

Solution by agitation without heat

Maltose may be dissolved in purified water by placing the formulations and also the ingredients are having extensive capacity through the volume of the syrup.

Advantage of syrups

- The active agent is homogeneously dispersed through the product.
- The active agent is in solution and does not need to undergo dissolution; therefore the therapeutic response is generally faster than if a tablet or capsule dosage form is used for treatment.
- The dose of the active agent is easily and conveniently adjusted by measuring adifferent volume. Syrups may be swallowed by patients who have difficulty taking tablets or capsules, as might be these with pediatric patients.
- Drugs such as potassium chloride that may cause ulceration to the mucosa in a tablet formulation avoid this side effect when present in solution.

Disadvantage of syrups

- The active ingredients, when present in solution, are usually more susceptible to chemical degradation, particularly hydrolysis, than when they are in solid dosage form.
- As a consequence of this, the solution product has a shorter shelf life than the solid formulation. Some pharmacologic agents taste or smell bad enough in solution that the patient has difficulty taking the medication.
- Liquid dosage forms are heavier and take up more shelf space than corresponding soild dosage sorms. If the container breaks, the product is irretrievably lost.

Methodology

1. Plant collection and Preparation of the plant extract:

Fresh Papaya and Euphorbia hitra leaves and plant parts were collected randomly from the various areas of Telangana, India. The leaves were separated and washed twice with double distilled water. The leaves were shade dried for 3 to 4 weeks. The leaves and plant parts were then subjected to extraction.

2.

3. Plant Extracts Preparation

Leaves of Papaya and Euphorbia hitra were dried for 3 to 4 weeks. Clean and dry Maceration Extraction process was taken. Then 25 gm of ground material and 250 ml of 95% dehydrated ethanol was filled in the apparatus and it was allowed to run till the completion of 6 cycles. After that the extract was collected and filtered using of standard filter paper for 48 hours. The filtrate was dried using of rotatory vacuum evaporator and the volume of the crude extract was reduced to 90% of its volume..All the extracts were kept in refrigerator prior to using.

4.

5. Formulation Development

Following ingredients were selected to develop the desired formulation

Table 1: Composition used in the formulation of syrups

S.No	Ingredient	F1	F2	F3	F4	F5	F6
1	Drug	2ml	2ml	2ml	2ml	2ml	2ml
2	Sucrose	2.5gm	2.5gm	2.5gm	2.5gm	2.5gm	2.5gm
3	Maltose	2.5gm	2.5gm	2.5gm	2.5gm	2.5gm	2.5gm
4	Glycerine	10ml	10ml	10ml	10ml	10ml	10ml
5	Propylene glycol	10ml	10ml	10ml	10ml	10ml	10ml
6	Distilled water	75ml	75ml	75ml	75ml	75ml	75ml

Development of Polyherbal Syrup

1. Preparation of Extracts

The collected papaya leaves (2kg) were dried and size reduced into coarse powder and macerated separately with 4ml of ethanol. After 7days of maceration both the extract was filtered out and concentrated under rotary vaccum evaporator. The residue was obtained and kept in a dessicator for the present study.

2. Preparation of Simple Syrup

Take 66.7gm of sucrose was weighed and added in to purified water heated until It dissolved with occasional stirring. Sufficing boiling water will be added to produce 100ml of simple syrup.

3. Preparation of Polyherbal Syrup

Take 1 gm of each extracts were dissolved in simple syrup IP and the volume was made upto 100ml by adding benzoic acid as preservative.

Results & Discussion

Disc Diffusion Method

The antibacterial activity of test compound was estimated by disc diffusion method. In this method glycerine polyethylene glycol were taken as test organisms was taken as standard molecule for antifungal activity.

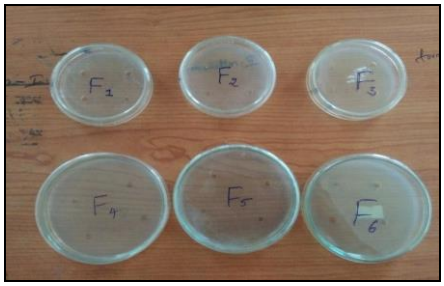

Fig 1: Zone of inhibition

Table 2: Measurments of Organisms activity

Organism	Name of the extract					
	Papaya	Euphorbia hitra	Glycerine	Ethanol	Distilled water	Group
K. Pneumonia	10mm	10mm	16 mm	2 mm	-	20 mm
E.Coli	10 mm	10 mm	12 mm	19 mm	19 mm	22 mm

The present study was aimed to developing ployherbal syrup using various polymers. All the formulations were evaluated for physicochemical properties and invitro drug release studies.

Analytical Method

Graphs of absorbance values of syrup (pH 1.2) and in p H 7.4 phosphate buffer at 228 nm and 232 nm respectively.

Table 3: Absorbance values of syrup

Concentration	Absorbance
0.5	0.158
1	0.326
1.5	0.477
2	0.640
2.5	0.849

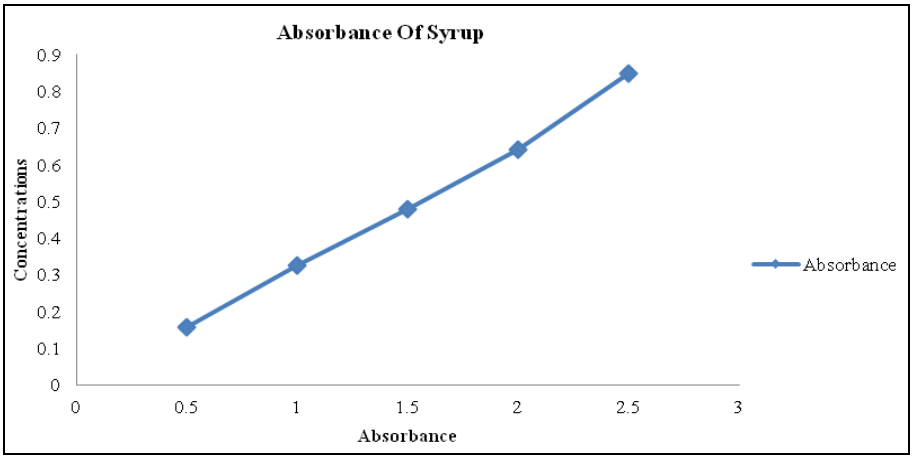

Fig 2: Absorbance of syrup

Study of different parameters of formulations

Table 4: Study of various parameters of different formulations

S NO	Formulation	pH	Specific Gravity	Viscosity Assay
1	F1	4.57	1.10	40.73
2	F2	4.34	1.14	34.45
3	F3	4.47	1.13	29.86
4	F4	4.47	1.11	26.97
5	F5	4.18	1.13	39.64
6	F6	4.84	1.12	58.15

The prepared polyherbal syrup were evaluated for the physical parameters such as pH, specific gravity , viscosity and all the results were found to be with in the pharmacoepial limits.

Table 5: Study of Stability tests of different formulations

S NO	Formulation	Color			Orour			Taste		
		DAY1	DAY15	DAY30	DAY1	DAY15	DAY30	DAY1	DAY15	DAY30
1	F1	Green	Light green	Light green	Pleasant	Pleasant	Pleasant	Sweet	Sweet	Sweet
2	F2	Green	Light green	Light green	Pleasant	Pleasant	Pleasant	Sweet	Sweet	Sweet
3	F3	Green	Light green	Light green	Pleasant	Pleasant	Pleasant	Sweet	Sweet	Sweet
4	F4	Green	Light green	Light green	Pleasant	Pleasant	Pleasant	Sweet	Sweet	Sweet
5	F5	Green	Light green	Light green	Pleasant	Pleasant	Pleasant	Sweet	Sweet	Sweet
6	F6	Green	Light green	Light green	Pleasant	Pleasant	Pleasant	Sweet	Sweet	Sweet

The prepared polyherbal syrup were evaluated for there stability studies such as color, odour, and taste and all the results were found to be were found to be with in the limits.

Table 6: Evaluation of ployherbal syrup by In-vitro permeation studies

Time (Hrs)	% Drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
0.5	12.31	12.98	12.36	12.06	12.10	11.11
1	19.53	21.71	25.2	19.8	18.68	20.21
2	20.78	31.9	32.7	27.48	27.50	28.01
3	35.5	40.8	48.3	38.1	39.3	39.3
4	45.7	44.7	44.4	46S.5	47.0	46.80
5	50.4	55.3	55.7	41.3	54.3	55.0
6	54.5	61.6	69.6	56.6	61.0	64.1
7	66.5	65.3	67.2	68.3	72.4	73.5
8	77.6	78.8	78.1	79.8	80.8	84.8

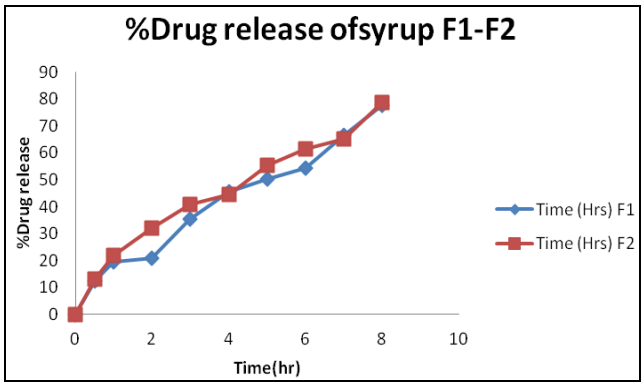

Fig 3:%Drug release of syrup F1-F2

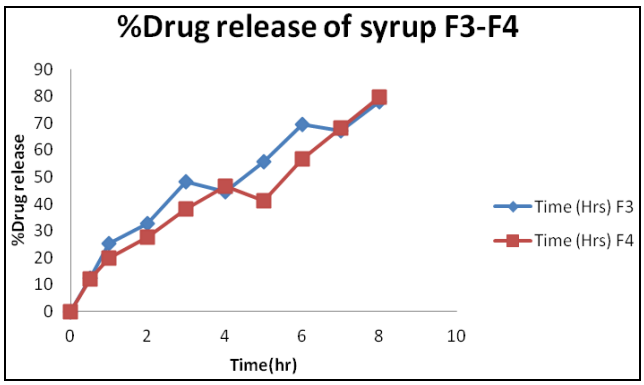

Fig 4: %Drug release of syrup F3-F4

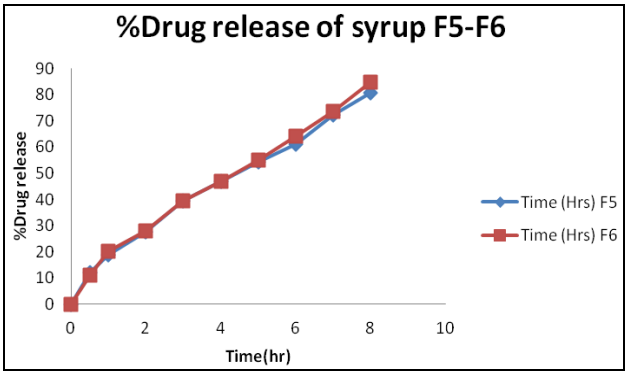

Fig 5:%Drug release of syrup F5-F6

The prepared were evaluated for the polyherbal syrup by In-vitro permeation studies using dialysis membrane, among all the 6 formulations F6 formulation was shown 84.8% cumulative drug release within 8 hours.

Conclusion

From the study which was carried out it was concluded that: The F6 batch was selected as the best formulation based on the various evaluation Studies. The results of this work suggest that the compound extracted from leaves are used for the treatment of dengue activity and this effect is increased by increasing the quantity of this compound. The crude leaves were collected from local forest which are then subjected for drying, extraction using maceration process. E. coli and S. pnemonia were used as test organisms in antibacterial testing of extract. Therefore, pharmacological test is necessary to isolate and characterize their active compounds. Moreover, these plants extract should be investigated in-vitro to better understand their safety, efficacy and properties. This extract used to prepare syrup, and evaluate purpose we are using various evaluation parameters of stability, viscosity- 58.15 centipoise, pH-4.84, specific gravity 1.14 and calculate the% drug release of syrup is 84.80% in 8hrs.

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